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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

DEJONG, ERIC S

ART UNIT

PAPER NUMBER

1631

NOTIFICATION DATE

DELIVERY MODE

03/24/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com  
pto@gbpatent.com

<b>Office Action Summary</b>	<b>Application No.</b> 09/810,670	<b>Applicant(s)</b> ITAI ET AL.	
	<b>Examiner</b> ERIC S. DEJONG	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,6,7,11 and 14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,6,7,11 and 14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED OFFICE ACTION**

Applicants response filed 12/12/2007 is acknowledged.

Claims 2-5, 8-10, 12, and 13 are canceled. Claim 14 is newly presented. Claims 1, 6, 7, 11, and 14 pending and currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendments made to the instant claims.

Claim 14 recites the limitation "the goodness of fit" in line 2 of said claim. There is insufficient antecedent basis for this limitation in the instant claim or in claims 1 and 7 from which claim 14 depends.

***Claim Rejections - 35 USC § 101***

The rejection of claims 12 and 13 under 35 USC § 101 are withdrawn in view of the cancellation of said claims.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 6, 7, 11, and 14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 6, 7, 11, and 14 are drawn to a method for selecting at least one lead-candidate compound capable of binding as a ligand to a protein. The method comprises the abstract/computational steps of inputting at least one query molecule known to bind, or is expected to bind, the protein, *in silico* screening of lead candidate compounds, estimating a binding scheme of the lead-candidate compounds and the query molecule to the protein based on three-dimensional information and outputting at least one lead-candidate compound and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation that results from said

application of judicial exception, thus the Examiner must determine if said application of a judicial exception produces a useful, concrete, and tangible result.

In determining if the application of a judicial exception produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a result to be "useful," the application of a judicial exception must produce a result that is specific, and substantial. For a result to be "concrete," the application of a judicial exception must have a result that is reproducible. For a result to be "tangible," the application of a judicial exception must produce a real world result . Furthermore, the claim must be limited only to statutory embodiments.

It is acknowledged that instant claims have been amended to now recite the step of "outputting... to a display, a user, a readily accessible memory, or other computer on a network" (see for example, lines 16 and 17 of instant claim 1) as suggest in the previous Office action (see page 4 of the Office action mailed 09/12/2007). Upon further reconsideration, the recited embodiments wherein a result (at least one lead-candidate compound) are output to a readily accessible memory or other computer on a network are considered transient computer embodiments that are not tangible. While it is acknowledged that the output of a result to a display or a user are considered tangible embodiments, the alternative embodiments of outputting a result to a readily accessible memory or a computer on a network causes the instant claims to encompass non-statutory embodiments. For the benefit of applicants, an amendment to the instant claims so as to remove the alternative embodiments of outputting to a readily accessible

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memory or a computer on a network would be sufficient to overcome the instant rejection.

### ***Response to Arguments***

Applicants' arguments filed 12/12/2007 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC §101 because the claimed invention is directed to non-statutory subject matter, applicants argue that the instant claims have been amended to recite "outputting... to a display, a user, a readily accessible memory, or other computer on a network" as suggested in the previous Office action.

In response, and as set forth in the above rejection, upon further reconsideration the recited embodiments wherein a result (at least one lead-candidate compound) are output to a readily accessible memory or other computer on a network are considered transient computer embodiments that are not tangible. Since the basis of the instant rejection has been changed by the examiner, this rejection has been treated as a new grounds of rejection that is not necessitated by applicants amendments to the instant claims.

***Claim Rejections - 35 USC § 102***

The rejection of claims 11 and 12 under 35 USC § 102(b) is withdrawn in view of the cancellation of said claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 7, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (IDS ref: J. Med. Chem. (1994) vol. 37, pp. 4479-4489).

The instant claims are drawn to a method for selecting at least one lead-candidate compound capable of binding as a ligand to a protein. The claimed method comprises the steps of inputting at least one query molecule known to bind or expected to be bound by the protein, screening lead-candidate compounds from a compound database by matching modes of covalent bonds between a query and trial compounds and judging similarities of partial structures of said compounds based on two-dimensional graphs, estimating a binding scheme of the lead-candidate compounds and the query molecule to the protein based on three-dimensional information and outputting at least one lead-candidate compound, and outputting at least one lead-candidate compound capable of binding the protein.

Wang et al. discloses a computer protein kinase C (PK-C) pharmacophore search on 206,876 nonproprietary structures in the NCI 3D-database that led to the

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discovery of five compounds which were found to possess PK-C binding affinities (see Wang et al., Abstract). Wang et al. disclose the construction of a PK-C pharmacophore query used in the 3D-database pharmacophoric search (see Wang et al., Figure 1) which is known to bind the PK-C receptor (see Wang et al., page 4480 col. 1, lines 1-17). The results of the computer implemented 3D-database pharmacophore search resulted in the identification of 535 that sufficiently matched the PK-C pharmacophore (see Wang et al., page 4480, col. 1, line 18 through col. 2, line 66). Wang et al. further disclose the visual inspection of 286 compounds of the 535 identified matches for the presence of hydrophobic constituents and further displays the 2D structures of 11 of said 286 compounds wherein atoms and covalent bonds are presented (see Wang et al., Figure 2 and page 4480, col. 2, lines 52-66). Wang et al. further disclose the computational molecular modeling study of known PK-C agonists containing a hydrophobic moiety and the use of this information in the qualitative selection of the final 125 compounds (see Wang et al., page 4480, col. 2, line 46-51 and page 4481, col. 2, line 1 through page 4486, col. 2, line 38). Wang et al. further discloses the synthesis and binding affinity testing of 125 identified compounds (see page 4481, col. 1, lines 1-12). Wang et al. further teaches the molecular modeling using the Quanta molecular modeling package (see Wang et al., page 4480, col. 2, lines 46-50) and detailed three-dimensional structure information of the PK-C receptor, lead compounds, and known PK-C agonists structures (see Wang et al., Table 3 and page 4479, col. 2, lines 10, page 4480, col. 1, lines 1-15, page 4482, col. 2, lines 18-41, page 4483, col. 1, line 1 through page 4484, col. 1, line 30). Wang et al. further teaches the estimation of a



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binding scheme between lead compounds, and known PK-C agonists structures to the PK-C receptor and determined that conformational changes of ligands upon binding on protein receptors do not have to be in their global or local energy minima to bind (see Wang et al., page 4485, col. 1, line 30 through page 4886, col. 1, line 9).

### ***Response to Arguments***

Applicants' arguments filed 12/12/2007/2007 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC § 102(b) as being anticipated by Wang et al., applicants argue that Wang et al. does not disclose estimating a binding scheme of the lead-candidate compounds to the protein. Applicants further argue that Wang et al. neither teaches nor suggests how the binding scheme of a lead-candidate compound to a protein may be estimated based on "correspondences of the mode of covalent binding of the partial structures of the query molecule and the trail molecules".

In response, it is first noted that the amendment to the instant claim 1 is directed to limitations that were previously presented in dependent claims 6 and 7 (see for example the claim set filed 06/14/2007). Further, it is reiterated from the instant rejection that Wang et al. further teaches the estimation of a binding scheme between lead compounds to known PK-C agonists structures of the PK-C receptor. Wang et al. further teaches the determination that conformational changes of ligands upon binding on protein receptors do not have to be in their global or local energy minima to bind (see Wang et al., page 4485, col. 1, line 30 through page 4886, col. 1, line 9). Contrary to

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applicant's argument, the determination of the effects conformational changes in modeled ligand structures following receptor binding, as taught by Wang et al., reads directly on estimating a binding scheme of lead-candidate compounds to a protein as instantly claimed. Further, the disclosed modeling of ligand conformations upon protein binding by Wang et al. reads directly on a correspondence of the mode of covalent bonds of partial structures of query and trail compounds as instantly claimed. Therefore it is maintained that Wang et al. fully anticipates the claimed invention.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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